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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,829	05/17/2006	Hiroshi Kase	00005.001293.	5752

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EXAMINER	
PIHONAK, SARAH	
ART UNIT	PAPER NUMBER
1627	
MAIL DATE	DELIVERY MODE
10/14/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,829	KASE ET AL.	
	Examiner	Art Unit	
	SARAH PIHONAK	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-5,9-12 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5,9-12 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application, filed on 5/17/2006, is a 371 (national stage application) of PCT/JP04/18765, filed on 12/9/2004.

Priority

The claim for foreign priority to Application No. 2003-410432, filed on 12/9/2003, was previously acknowledged in the office action dated 3/30/2009.

Response to Arguments

In the office action dated 3/30/2009, claims 6-8 were rejected under 35 USC § 103(a) as being unpatentable over Shimada et. al., US Patent No. 6,727,259, in view of Middleton et. al., Brain Res. Rev., 31, pp. 236-250, and Graybiel, Current Opin. Neurobiol., pp. 733-741. In the response filed on 7/28/2009, claims 6-8 were cancelled; therefore the rejection of these claims is moot. Claims 9-12 were objected to; the Applicants' arguments regarding the objection of these claims has been found persuasive, and the objection to these claims is withdrawn. In addition to claims 6-8, claims 1 and 13-15 have been cancelled by the Applicant. New claim 16 has been added.

The rejection of claims 6-8 for nonstatutory obviousness type double patenting over claims 2-3 of US Patent No. 6,727,259 is considered moot. In further consideration of the claims, new rejections under 35 USC § 103(a), 35 USC § 112, and under nonstatutory obviousness type double patenting have been made, which will be discussed further in this office action. Accordingly, this action is made **NON-FINAL**.

Claims 2-5, 9-12, and 16 have been examined with regards to the previously elected

species of formula (I), (E)-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methylxanthine, also known as KW 6002.

1. Claims 2-5, 9-12, and 16 were examined.

2. Claims 2-5, 9-12, and 16 are rejected.

Claim Rejections-35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 2-5, 9-12, and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of higher brain function impairments such as memory, action, and learning, does not reasonably provide enablement for prevention of such impairments. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. See M.P.E.P. 2164.08. The reference of Small, *British Medical Journal*, **324**, pp. 1502-1505, is used in this rejection.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not

be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to treatment and prevention of an impairment of higher brain functioning, such as learning, memory, recognition, and action. Thus, the claims taken together with the specification imply that impairments of learning, memory recognition, and action can be prevented. The term prevention has an absolute meaning, in which it is implied that the event can be kept from occurring, under all circumstances. Therefore, the claims are broad in scope, in that they are not only drawn to treatment of such impairments, but are also drawn to keeping such impairments from occurring.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The prior art suggests that while impairments in cognitive functioning such as memory and learning can be reduced, prevention has not yet been achieved. Small teaches that the likelihood of developing memory loss increases with age, and that approximately 40% of people aged 65 and older experience memory impairment in the United States (p. 1502, left column, first and third paragraphs). Additionally, the risk of developing diseases associated with cognitive decline such as Alzheimer's increases with age (p. 1502, right column, first paragraph). Small teaches that there are multiple factors involved in the development of impaired cognitive function, such as family history, lifestyles, and health (p. 1502, right column, second full paragraph; p. 1503, right column, top paragraph). It is taught that prolonged stress leads to impairments in memory and learning, and that intellectual stimulation has been shown to reduce the risk of developing such impairments (p. 1503, right column, last paragraph-p. 1504, left column, top paragraph; p. 1504, right column, paragraphs under "Mental activity"). Additionally, smoking and obesity are associated with an increase in development of cognitive impairments (p. 1504, left column, last paragraph; p. 1505, left column, first full paragraph). Therefore, Small teaches that there are a variety of factors that determine the likelihood of developing cognitive impairments associated with memory and learning. Some of these factors, such as advanced age and heredity, can not be eliminated. While an individual can take steps which will likely reduce their risk of developing memory and learning impairments, it is not possible to prevent them.

(5) The relative skill of those in the art:

The relative skill of one in the art is expected to be high, such as that of an MD or PhD.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for treatment of impairment of higher cognitive functioning, such as learning, memory, action, and other skills.

However, the specification does not provide guidance for prevention of impairment of learning, memory, action, and other cognitive skills.

(8) The quantity of experimentation necessary:

5. Considering the state of the art as discussed by the references above, particularly with regards to the evidence provided by the prior art and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Claim Rejections-35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

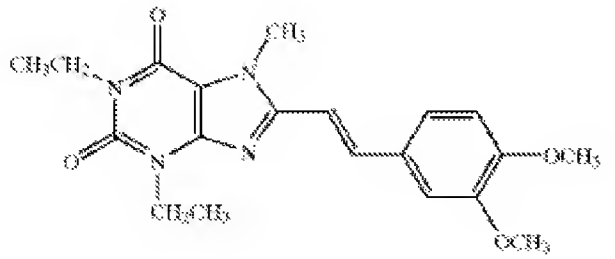
7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 2-5, 9-12, and 16 rejected under 35 U.S.C. 103(a) as being unpatentable over Shimada et. al., EP 1016407 patent publication, in view of Ikeda et. al., *Behavioral Brain Research*, **118**, pp. 17-25.

The claims are directed to a method of treating an impairment of higher brain dysfunction such as memory and learning, comprising administration of the elected species, KW 6002, which is shown below:



Shimada et. al. teaches that xanthine compounds such as KW 6002 are effective for treating neurodegenerative disorders, including Alzheimer's disease, propagating spongy brain fever, brain ischemia, and others (p. 2, paragraph [0001]; p. 5, Table 1, compound No. 1, lines 5-10, and lines 35-40; p. 8, paragraph [0028]).

While Shimada et. al. teaches that KW 6002 is effective for treating neurodegenerative disorders and brain ischemia, it is not explicitly taught as a treatment for higher brain dysfunctions such as memory, learning, and other cognitive skills.

Ikeda et. al. teaches that ischemic brain damage results in considerable long lasting learning and memory impairment (Abstract). Ikeda et. al. teaches that in subjects who were afflicted with cerebral ischemia, learning of new tasks and spatial cognition were impaired (p. 20, right column, full paragraphs 2-3). It is also taught that attention deficits were observed in these subjects, and that learning abnormalities and impairments in long-term memory and reference memory were apparent (p. 23, right column, first full paragraph; p. 24, right column, last two paragraphs).

Shimada et. al. teaches that KW 6002 is effective in treating neurodegenerative diseases and conditions, including brain ischemia, and Ikeda et. al. teaches that brain ischemia results in pronounced deficits involving learning and memory. It would have been prima facie obvious for one of ordinary skill in the art, at the time of the invention,

to treat a patient suffering from learning and memory impairments with KW 6002, because it is taught that this agent is effective for treating neurodegenerative conditions such as brain ischemia, which is associated with learning and memory impairments. Therefore, one of ordinary skill in the art would have expected success in treating learning and memory impairments with KW 6002, because the prior art teaches that this compound is effective in treating a condition which is associated with these impairments. Additionally, amnesia is defined as a partial or total loss of memory (http://www.credoreference.com/search.do?query=amnesia&subject=all&scope=title&title=502&view=facet). As Ikeda et. al. teaches that memory impairment, and therefore amnesia, is associated with brain ischemia, it would have been prima facie obvious for one of ordinary skill in the art to administer KW 6002 to treat amnesia.

Claim Rejections-Obviousness Type Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 2-5, 9-12, and 16 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 7115614 in view of Ikeda et. al., *Behavioral Brain Res.*, **118**, pp. 17-25.

The claims are drawn to treatment of higher brain cognitive impairments involving learning and memory, with the elected compound KW 6002. Claim 1 of the US Patent No. 7,115,614 is drawn to treatment of brain ischemia, comprising administration of KW 6002. Ikeda et. al. teaches that brain ischemia is associated with impairments in learning and memory (p. 23, right column, first full paragraph; p. 24, right column, last two paragraphs). Therefore, as impairments in learning and memory are associated with brain ischemia, one of ordinary skill in the art would have expected that in treating brain ischemia, the learning and memory impairments associated with brain ischemia would also have been treated with KW 6002. Therefore, the claims are not patentably distinct from each other.

12. Claims 2-5, 9-12, and 16 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,727,259.

The claims are drawn to treatment of higher brain cognitive impairments involving learning and memory, with the elected compound KW 6002. Claims 1-3 of the US Patent No. 6,727,259 are drawn to treatment and inhibition of neurodegenerative disorders, including Alzheimer's disease, comprising administration of KW 6002. It is

well known in the art that Alzheimer's disease is marked by a progressive decline in cognitive function, including memory and learning (http://www.merck.com/mmhe/sec06/ch083/ch083c.html#sec06-ch083-ch083c-522). Therefore, as the instant claims are drawn to treating impairments in memory and learning, and these impairments are associated with neurodegenerative conditions such as Alzheimer's disease, both sets of claims are not patentably distinct from each other.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is (571)270-7710. The examiner can normally be reached on Monday-Thursday 8:00 AM - 6:30 PM EST, with Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S.P.

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627